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FILE COVERS 1907 - 14 Jul 2008  VOL 149 ISS 3
FILE LAST UPDATED: 13 Jul 2008  (20080713/ED)

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reclassification data for the second quarter of 2008.

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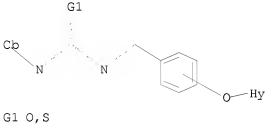


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G1 O,S


Structure attributes must be viewed using STN Express query preparation.
L3           77 SEA FILE=REGISTRY SSS FUL L1
L4            7 SEA FILE=CAPLUS L3


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L4   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2006:218143  CAPLUS
DOCUMENT NUMBER:          144:292764
TITLE:                    Preparation of aminotetrazoles analogues as P2X7
                          purinoreceptor antagonists for the treatment of
                          inflammatory and neuropathic pain
INVENTOR(S):              Carroll, William A.; Perez-Medrano, Arturo;
                          Florjancic, Alan S.; Nelson, Derek W.; Peddi, Sridhar;
                          Li, Tongmei; Bunnelle, Eric M.; Hirst, Gavin; Li,
                          Biquin C.
PATENT ASSIGNEE(S):       USA
```

SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S. Ser. No. 120,718.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060052374	A1	20060309	US 2005-221333	20050907
US 20070049584	A1	20070301	US 2005-120718	20050429
PRIORITY APPLN. INFO.:			US 2004-566238P P	20040429
			US 2005-120718 A2	20050429

OTHER SOURCE(S): MARPAT 144:292764
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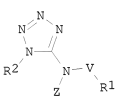
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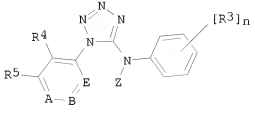
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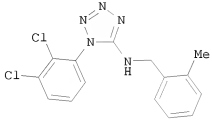
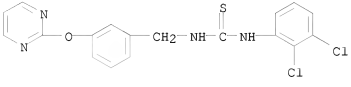

III

AB Title compds. I and II [R2 = (un)substituted Ph, pyridinyl; V = (CXY)m; m = 0-3; X, Y, Z = independently H, alkyl; CXY = ring selected from (un)substituted cyclopropane, cyclohexane, piperidine, etc.; Z and X together with the atoms to which they are attached may form a ring selected from pyrrolidine, piperidine, piperazine, etc.; R1 = Ph, adamantyl, pyridyl, etc.; A, B, E = independently N and (un)substituted CH; R3 = (un)substituted alkyl, amino, etc.; n = 1-3; when n = 2-3, R3 may be the same or different; R4 = halo, NH2, alkyl, etc.; R5 = H, halo, NH2, etc.; and therapeutically acceptable salts, solvates, prodrugs, or salts of prodrugs thereof; with limitations and the exception of certain compds.] were prepared as P2X7 purinoreceptor antagonists. For example, addition of 2,3-dichlorophenyl isothiocyanate with 2-methylbenzylamine in THF for 1 h at room temperature followed by cyclization with sodium azide in the presence of mercuric acetate at room temperature for 16 h gave tetrazole III.
I
demonstrated antagonist activity at the P2X7 receptor in vitro with IC50 < 10 μM. Thus, I are useful for treating chronic inflammatory and neuropathic pain, neurodegeneration, spinal cord injury, and depression.

IT 870062-24-1P, 1-(2,3-Dichlorophenyl)-3-[3-[(pyrimidin-2-yl)oxy]benzyl]thiourea
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of aminotetrazoles analogs as P2X7 purinoreceptor antagonists for treatment of inflammatory and neuropathic pain)
RN 870062-24-1 CAPLUS
CN Thiourea, N-(2,3-dichlorophenyl)-N'-[[3-(2-pyrimidinyloxy)phenyl]methyl]- (CA INDEX NAME)



L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1241277 CAPLUS
DOCUMENT NUMBER: 144:6791
TITLE: Preparation of aminotetrazoles analogues as P2X7 purinoreceptor antagonists for the treatment of inflammatory and neuropathic pain
INVENTOR(S): Carroll, William A.; Perez-Medrano, Arturo; Florjancic, Alan S.; Nelson, Derek W.; Peddi, Sridhar; Bunnelle, Eric M.; Hirst, Gavin C.; Li, Biqin
PATENT ASSIGNEE(S): Abbott Laboratories, USA; Li, Tongmei
SOURCE: PCT Int. Appl., 345 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005111003	A1	20051124	WO 2005-US14641	20050428
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2565211	A1	20051124	CA 2005-2565211	20050428
EP 1747206	A1	20070131	EP 2005-744712	20050428
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007535553	T	20071206	JP 2007-510981	20050428
MX 2006PA12595	A	20070509	MX 2006-PA12595	20061030
PRIORITY APPLN. INFO.:			US 2004-566238P P	20040429
			WO 2005-US14641 W	20050428

OTHER SOURCE(S): MARPAT 144:6791
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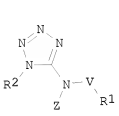

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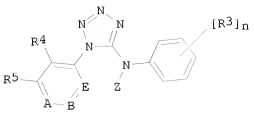

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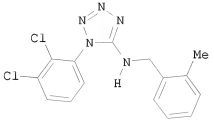


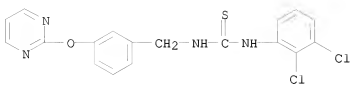
III

AB Title compds. I and II [R2 = (un)substituted Ph, pyridinyl; V = (CXY)m; m = 0-3; X, Y, Z = independently H, alkyl; CXY = ring selected from (un)substituted cyclopropane, cyclohexane, piperidine, etc.; Z and X together with the atoms to which they are attached form a ring selected from pyrrolidine, piperidine, piperazine, etc.; R1 = Ph, adamantyl, 2,3-dihydrospiroindene-1,4'-piperidinyl, etc.;A, B, E = independently N, CH and derivs.; R3 = (un)substituted alkyl; v = 0,2,3; when v = 2-3, R3 may be the same or different; R4 = Cl, F, Nr, I, NH2, etc.; R5 = H, CN, Cl, Br, NH2, etc.; and therapeutically acceptable salts, solvates, prodrugs, or salts of prodrugs thereof; with the exception of certain compds.] were prepared as P2X7 purinoreceptor antagonists. Thus, addition of mercuric acetate and sodium azide to a prestirred mixture of 2-methylbenzylamine and 2,3-dichlorophenyl isothiocyanate in THF gave tetrazole III. I demonstrated antagonist activity at the P2X7 receptor in vitro with IC50 < 10 μM. Thus, I are useful for treating chronic inflammatory and neuropathic pain, neurodegeneration, spinal cord injury, and depression.

IT 870062-24-1P, 1-(2,3-Dichlorophenyl)-3-[3-[(pyrimidin-2-yl)oxy]benzyl]thiourea
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of aminotetrazoles analogs as P2X7 antagonists for treatment of inflammatory and neuropathic pain)

RN 870062-24-1 CAPLUS

CN Thiourea, N-(2,3-dichlorophenyl)-N'-[[3-(2-pyrimidinyloxy)phenyl]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:216619 CAPLUS
DOCUMENT NUMBER: 142:297864
TITLE: Preparation of aniline derivatives and related compounds as c-kit modulators
INVENTOR(S): Cheng, Wei; Co, Erick Wang; Kim, Moon Hwan; Klein, Rhett Ronald; Le Donna, T.; Lew, Amy; Nuss, John M.; Xu, Wei; Bajjalieh, William
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020921	A2	20050310	WO 2004-US28001	20040827
WO 2005020921	A3	20051006		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004268621	A1	20050310	AU 2004-268621	20040827
CA 2536954	A1	20050310	CA 2004-2536954	20040827
EP 1663204	A2	20060607	EP 2004-782473	20040827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007504160	T	20070301	JP 2006-524905	20040827
US 20080096892	A1	20080424	US 2007-569873	20070904

PRIORITY APPLN. INFO.: US 2003-499224P P 20030829
WO 2004-US28001 W 20040827

OTHER SOURCE(S): MARPAT 142:297864
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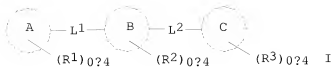

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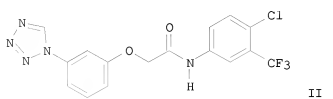


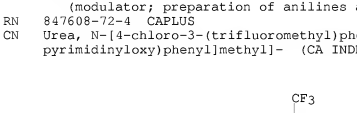
II

AB Compds. I [wherein ring A is a five- to fourteen-membered heteroaryl; R1, R2 and R3 are H, halo, trihalomethyl, cyano, nitro, etc.; L1 is a single bond, (un)substituted alkylene, O, CH2O, etc.; ring B is five- to ten-membered aryl or heterocyclyl; ring C is five- to ten-membered (hetero)aryl; L2 is alkylene, alkylidene, alkylidyne, etc.; with some limitations and exclusions, and pharmaceutically acceptable salts, hydrates or prodrugs thereof], as exemplified by carbonyl compds. of anilines, were prepared as c-Kit kinase modulators. For example, 3-aminophenoxyacetic acid, which was obtained from the corresponding nitro compound in 76% yield via catalytic hydrogenation, was treated with HC(OEt)3 and NaN3 in AcOH followed by NaNO2/HCl to give a tetrazole in 61% yield. This acid was coupled with 5-amino-2-chlorobenzotrifluoride in the presence of HATU to afford acetamide II in 46% yield, which showed inhibition against c-Kit kinase with a IC50 of < 50 nM. Therefore, I and pharmaceutical compns. thereof are useful for modulating c-Kit kinase activity and for treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities.

IT 847608-72-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modulator; preparation of anilines and related compds. as C-kit modulators)

RN 847608-72-4 CAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[[4-(2-pyrimidinyloxy)phenyl]methyl]- (CA INDEX NAME)



L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:370904 CAPLUS

DOCUMENT NUMBER: 140:391200

TITLE: Preparation of pyridinyloxybenzylureas as RAF kinase inhibitors.

INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Schadt,

Oliver; Amendt, Christiane; Zenke, Frank; Sirrenberg, Christian; Grell, Matthias; Finsinger, Dirk

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 341 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

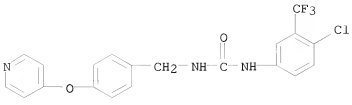
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037789	A2	20040506	WO 2003-EP11134	20031008
WO 2004037789	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503445	A1	20040506	CA 2003-2503445	20031008
AU 2003268926	A1	20040513	AU 2003-268926	20031008
EP 1562905	A2	20050817	EP 2003-750697	20031008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015580	A	20050830	BR 2003-15580	20031008
CN 1705645	A	20051207	CN 2003-80101925	20031008
JP 2006506454	T	20060223	JP 2005-501513	20031008
MX 2005PA04206	A	20050608	MX 2005-PA4206	20050420
US 20060199844	A1	20060907	US 2005-532574	20050425
ZA 2005004175	A	20060329	ZA 2005-4175	20060117

PRIORITY APPLN. INFO.:
EP 2002-23906 A 20021024
US 2003-490285P P 20030728
WO 2003-EP11134 W 20031008

OTHER SOURCE(S): MARPAT 140:391200

AB ADB [D = methyleneurea moiety or derivative thereof; A = (substituted) L(ML')a; L = 5-7 membered cyclic structure, e.g. aryl, heteroaryl, arylene, heteroarylene; L' = (substituted) cyclic moiety having ≥5 members, e.g. aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group having ≥1 atom; a = 1-4; B = (substituted) up to tricyclic aryl, heteroaryl], were prepared for treatment of hyperproliferative and nonproliferative disorders (no data). Thus, 4-(4-pyridinyloxy)benzylamine (preparation given) and 4-chloro-3-trifluoromethylphenyl isocyanate were stirred together for 2 h in CH2Cl2 to give 1-(4-chloro-3-trifluoromethylphenyl)-3-[4-(4-pyridinyloxy)benzyl]urea.

IT 685533-65-7P 685533-66-8P 685533-67-9P
685533-68-0P 685533-71-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methylene urea derivs. as RAF kinase inhibitors)
RN 685533-65-7 CAPLUS
CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[[4-(4-pyridinyloxy)phenyl]methyl]- (CA INDEX NAME)



RN 685533-66-8 CAPLUS
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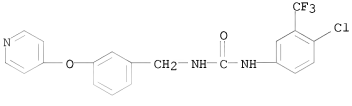
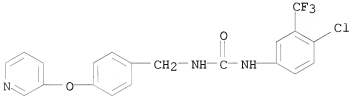


RN 685533-67-9 CAPLUS
CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[[4-(3-pyridinyloxy)phenyl]methyl]- (CA INDEX NAME)



RN 685533-68-0 CAPLUS
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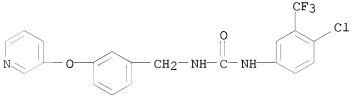

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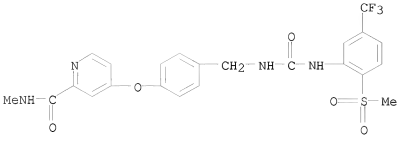

IT 685534-00-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of methylene urea derivs. as RAF kinase inhibitors)
RN 685534-00-3 CAPLUS
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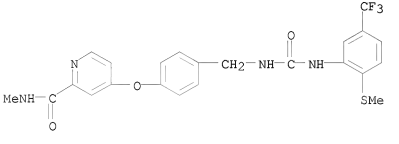


L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:664665 CAPLUS
DOCUMENT NUMBER: 135:366322
TITLE: Selective inhibition of ICAM-1 and E-selectin expression in human endothelial cells. 2. Aryl modifications of 4-(aryloxy)thieno[2,3-c]pyridines with fine-tuning at C-2 carbamides
AUTHOR(S): Zhu, Gui-Dong; Arendsen, David L.; Gunawardana, Indrani W.; Boyd, Steven A.; Stewart, Andrew O.; Fry, Dennis G.; Cool, Barbara L.; Kifle, Lemma; Schaefer, Verlyn; Meuth, Joseph; Marsh, Kennan C.; Kempf-Grote, Anita J.; Kilgannon, Patrick; Gallatin, W. Michael; Okasinski, Gregory F.
CORPORATE SOURCE: Metabolic Diseases Research Pharmaceutical Products Division Department 04MJ, Abbott Laboratories, Abbott Park, IL, 60064-6101, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(21), 3469-3487
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:366322
AB The elevated expression of cell adhesion mols. (CAMs) on the lumenal surface of vascular endothelial cells is a critical early event in the complex inflammatory process. The adhesive interactions of these CAMs

that include E-selectin, ICAM-1, and VCAM-1 with their counter-receptors on leukocytes, such as integrins of the αLβ2 family, result in migration of the leukocytes to the site of inflammation and cause tissue injury. Pharmaceutical agents that could suppress the induced expression of one or more of these cell adhesion mols. would provide a novel mechanism to attenuate the inflammatory responses associated with chronic inflammatory diseases. A-205804, a potent and selective inhibitor of the induced expression of E-selectin and ICAM-1 over VCAM-1, was further modified with emphasis at the C-4 and C-2 positions to identify a more potent drug candidate with a good pharmacokinetic profile and phys. properties. Replacement of the C-4 sulfur linkage in A-205804 with an oxygen atom eliminated one of the two major metabolites for this lead mol. The para-position of the 4-phenoxy group of the thieno[2,3-c]pyridine lead is found to be very critical for a higher in vitro potency and selectivity of E-selectin and ICAM-1 over VCAM-1 expression. This position is presumably close to the solvent-accessible region of the target protein-inhibitor complex. An attempt to install a water-solubilizing group at the para-position of the phenoxy group to increase the aqueous solubility of this lead

series through various linkages failed to provide an ideal inhibitor. Only small substituents such as fluorine are tolerated at the meta- and ortho-positions of the 4-phenoxy to retain a good in vitro potency. Bromo, trifluoromethyl, pyrazol-1-yl, and imidazol-1-yl are among the better substituents at the para-position. With fine-tuning at the C-2 position we discovered a series of very potent (IC50 < 5 nM for ICAM-1) and selective (>200-fold vs. VCAM-1) inhibitors with a good pharmacokinetic profile. Demonstrated efficacy in a rat rheumatoid arthritis model and in a mice asthma model with selected compds. is also reported.

IT 373633-41-1P

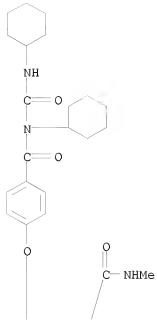
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(selective inhibition of ICAM-1 and E-selectin expression in human endothelial cells: aryl modifications of aryloxythienopyridines with fine-tuning at C-2 carbamides)

RN 373633-41-1 CAPLUS

CN Thieno[2,3-c]pyridine-2-carboxamide, 4-[4-[[cyclohexyl[(cyclohexylamino)carbonyl]amino]carbonyl]phenoxy]-N-methyl- (CA INDEX NAME)

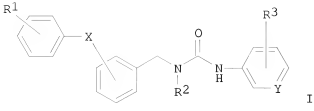
PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:102442 CAPLUS
DOCUMENT NUMBER: 128:238966
ORIGINAL REFERENCE NO.: 128:47129a,47132a
TITLE: Inhibitors of acyl-CoA:cholesterol O-acyltransferase (ACAT). Part 1: identification and structure-activity relationships of a novel series of substituted N-alkyl-N-biphenylylmethyl-N'-arylureas
AUTHOR(S): Tanaka, Akira; Terasawa, Takeshi; Hagihara, Hiroyuki; Sakuma, Yuri; Ishibe, Noriko; Sawada, Masae; Takasugi, Hisashi; Tanaka, Hirokazu
CORPORATE SOURCE: Medicinal Chemistry Research Laboratories, Fujisawa Pharmaceutical Co. Ltd., Osaka, 532, Japan
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(1), 15-30
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



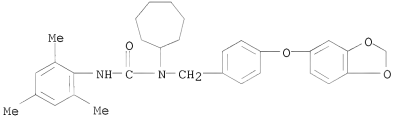
I

AB A series of N-alkyl-N-biphenylylmethyl-N'-arylurea and related derivs. (I) were prepared and evaluated for their ability to inhibit acyl-CoA:cholesterol O-acyltransferase in vitro and to lower plasma cholesterol levels in cholesterol-fed rats in vivo. Linking of two Ph groups via oxygen and introduction of fluorine at appropriate positions on the biphenyl moiety improved in vitro and in vivo activity. From this series of analogs, compound 40 (FR179254), which had potent in vitro potency (rabbit intestinal microsomes IC50 = 25 nM), showed excellent plasma cholesterol-lowering activity when administered via the diet (ED50 = 0.045 mg/kg). However, the hypocholesterolemic effect of this compound was moderate when dosed by oral gavage in PEG400 as a vehicle (ED50 = 5.3 mg/kg). Modification of the N'-aryl moiety led to the identification of compound 50 (FR182980) which was efficacious in both dosing models (ED50 = 0.034 mg/kg and 0.11 mg/kg, resp.). steroids.

IT 179054-10-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity relationships of N-alkyl-N-biphenylylmethyl-N'-arylureas as anticholesteremics and acyl-CoA:cholesterol O-acyltransferase inhibitors)

RN 179054-10-5 CAPLUS

CN Urea, N-[[4-(1,3-benzodioxol-5-yloxy)phenyl]methyl]-N-cycloheptyl-N'-(2,4,6-trimethylphenyl)- (CA INDEX NAME)



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:455768 CAPLUS

DOCUMENT NUMBER: 125:114322

ORIGINAL REFERENCE NO.: 125:21442h,21443a

TITLE: Preparation of urea derivatives as cholesterol acyltransferase inhibitors

INVENTOR(S): Terasawa, Takeshi; Tanaka, Akira; Chiba, Toshiyuki; Takasugi, Hisashi

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 228 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610559	A1	19960411	WO 1995-JP1982	19950929
W: AU, CA, CN, HU, JP, KR, MX, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
IN 1995MA01229	A	20050225	IN 1995-MA1229	19950922
CA 2200981	A1	19960411	CA 1995-2200981	19950929
AU 9535779	A	19960426	AU 1995-35779	19950929
EP 784612	A1	19970723	EP 1995-932934	19950929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10510512	T	19981013	JP 1995-511616	19950929
ZA 9508365	A	19960508	ZA 1995-8365	19951004
PRIORITY APPLN. INFO.:			GB 1994-19970	A 19941004
			GB 1995-6720	A 19950331
			GB 1995-14021	A 19950710
			WO 1995-JP1982	W 19950929

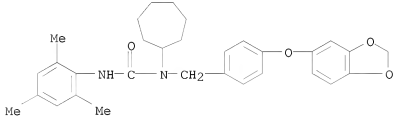
OTHER SOURCE(S): MARPAT 125:114322

AB R4YC6H4(CH2)nNR2CONHR3 [R2 = (ar)alkyl, heterocyclyl(alkyl), alkoxyalkyl, etc.; R3,R4 = (un)substituted aryl, heterocyclyl; Y = bond, alkylene, O, CO, CONH, etc.; n = 0 or 1] were prepare Thus, 1-cycloheptyl-1-(4-phenoxyphenylmethyl)-3-(2,4,6-trifluorophenyl)urea had IC50 of 1.1x10-8M against cholesterol acyltransferase in vitro.

IT 179054-10-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. as cholesterol acyltransferase inhibitors)

RN 179054-10-5 CAPLUS

CN Urea, N-[[4-(1,3-benzodioxol-5-yloxy)phenyl]methyl]-N-cycloheptyl-N'-(2,4,6-trimethylphenyl)- (CA INDEX NAME)



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